ADVISORY COMMITTEE FOR PHARMACEUTICAL SCIENCE

May 7-8, 2002

CDER Advisory Committee Conference Room
5630 Fishers Lane, Rockville, MD

Questions

Food Effect BE Studies

1. With regard to waiver of *in vivo* fed bioequivalence (BE) studies in Abbreviated New Drug Applications (ANDAs) for BCS Class I drugs/drug products:

1.1 To what extent does the committee feel that the literature, in-house and original research data provide sufficient evidence to support the claim that 1. With regard to waiver of *in vivo* fed bioequivalence (BE) studies in Abbreviated New fed BE studies are unnecessary?

1.2 If additional evidence were needed to support the waiver of *in vivo* fed BE studies for BCS Class I drug/drug products, what form of evidence would be desirable?

2. With regard to using confidence intervals and a criterion to claim bioequivalence between fasted and fed states for new drugs and between fed states for generic drugs (relative to reference products):

2.1 To what extent does the committee feel that the issue of food effects can be treated as a lack of equivalence question?

2.2 To what extent does the committee feel that a 90% confidence interval with boundaries of 80-125% are appropriate to make a claim of bioequivalence?

2.3 What alternative approaches would the committee suggest to demonstrate bioequivalence in the fed state?

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Scientific Basis for Current BCS Based Biowaivers

(1) Should the Agency consider expanding the application of BCS based biowivers to rapidly dissolving conventional (IR) products of Class III (high solubility and low permeability) drugs? If so, what evidence should the agency collect to justify this extension?

(2) Should the Agency consider expanding the application of BCS based biowivers of conventional (IR) solid oral products of Class II (low solubility and high permeability) drugs that exhibit similar in vitro dissolution? If so, what evidence should the agency collect to justify this extension?

Blend Uniformity

Do you consider the PQRI proposal appropriate for inclusion in a planned revised FDA guidance? If no, please suggest modifications or improvements.

If yes, should the proposed stratified sampling and analysis plan be applicable only for the bioequivalence batch and validation batches?

If the proposed stratified sampling and analysis plan is limited only to bioequivalence and validation batches, how should adequacy of mix be ensured for routine production batches?

Should the planned revised FDA guidance only focus on generic drugs or should it be a general guidance (i.e., for both new and generic drugs)?